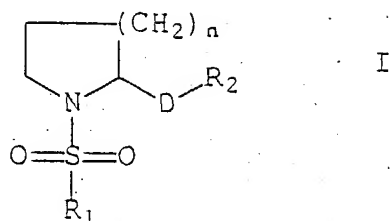


What is claimed is:

1. A compound having the formula (I):



where

n is 1-3;

R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere;

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or CO<sub>2</sub>R<sup>4</sup> where R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl;

or a pharmaceutically acceptable salt, ester or solvate thereof;

provided that:

when D is a bond, and  $R_2$  is COOH,  
then  $R_1$  cannot be substituted naphthyl;  
further provided that:

when D is a bond, and n is 1, and  $R_2$  is COOH or CONHR<sub>3</sub>,  
then  $R_1$  is not hydroxyl, methyl, ethyl, substituted or  
unsubstituted thioethyl, benzothiazole, substituted  
benzopyran, substituted benzopyrrole, substituted  
benzoxazole, substituted 5-membered heterocycle  
containing two N and one S heteroatoms, or substituted  
or unsubstituted phenyl, phenylethyl, naphthyl, pyridyl,  
thienyl, quinoline, tricyclic ring, aminoethyl, or  
benzyl;

further provided that:

when D is a bond, and n is 2, and  $R_2$  is COOH or  
phenylbutyl ester,  
then  $R_1$  is not substituted phenyl, or a substituted  
bicyclic ring containing two oxygen heteroatoms.

further provided that:

when D is a bond, and n is 1-2, and  $R_2$  is a substituted  
or unsubstituted carbocyclic or heterocyclic ring  
structure,

then  $R_1$  is not substituted or unsubstituted carbocycle  
or heterocycle, or hydroxy;

further provided that:

when D is a bond, and n is 1-2, and  $R_2$  is hydroxy,  
alkoxy,  $-SO_2(\text{phenyl})$ ,  $N(R_3)_2$ , substituted thio or  
alkylthio,  $-NCO$ ,  $-PO_3(\text{Me})_2$ , or  $-NCOOC(\text{ethyl})\text{phenyl}$ ,  
then  $R_1$  is not naphthalene, ethylene, substituted  
tricyclic ring, or substituted or unsubstituted phenyl;

further provided that:

when D is  $C_1-C_3$  alkyl or hexenyl, and  $R_2$  is hydroxyl,  
then  $R_1$  is not substituted or unsubstituted phenyl, or  
benzoimidazole;

further provided that:

when D is methyl, and n is 1, and  $R_2$  is cyano or COOH,

then R<sub>1</sub> is not substituted phenyl;

further provided that:

when D is methyl, and n is 1, and R<sub>2</sub> is methoxy or N(R<sub>3</sub>)<sub>2</sub>,

5 then R<sub>1</sub> is not methyl, ethyl, phenylethyl, chloro substituted alkyl, substituted oxirane, substituted aziridine wherein one of the carbons is replaced with an oxygen, substituted or unsubstituted propenyl, substituted phenyl, benzyl, or trifluoro substituted C<sub>2</sub>-  
10 C<sub>3</sub> alkyl or alkenyl;

further provided that:

when D is ethyl, and n is 2, and R<sub>2</sub> is hydroxyl or N(R<sub>3</sub>)<sub>2</sub>,

then R<sub>1</sub> is not naphthyl;

15 further provided that:

when D is propyl, and n is 1, and R<sub>2</sub> is methoxy,

then R<sub>1</sub> is not ethylene, cyano substituted ethyl, or triethoxy substituted propyl;

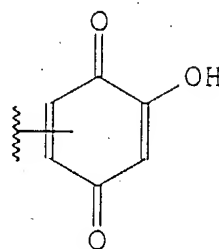
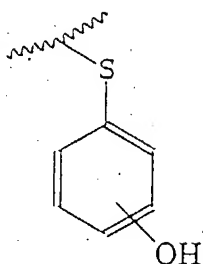
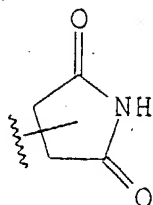
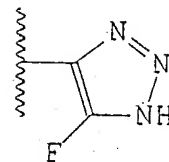
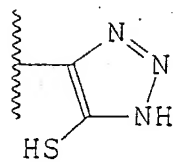
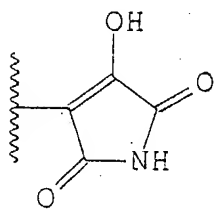
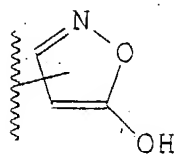
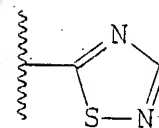
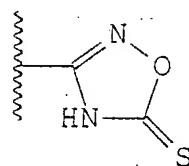
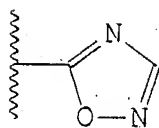
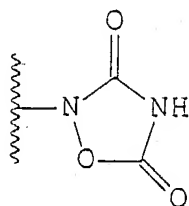
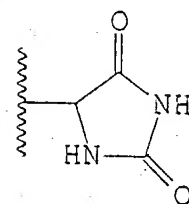
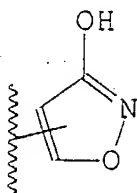
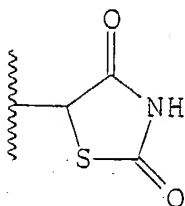
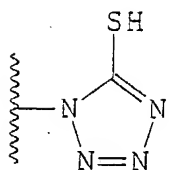
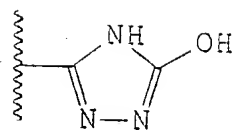
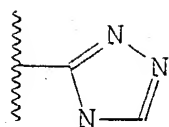
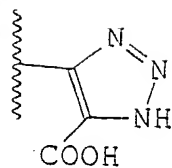
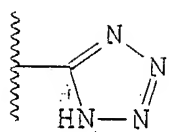
further provided that:

20 when D is not a bond and at least one of D and R<sub>2</sub> contains at least one S or O,

then R<sub>1</sub> is not methyl or substituted phenyl.

25 2. The compound of claim 1, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R<sup>3</sup>.

30 3. The compound of claim 1, wherein R<sub>2</sub> is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

4. The compound of claim 1, wherein the carboxylic acid or carboxylic acid isostere of  $R_2$  is selected from the group consisting of:

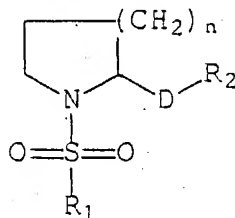
$-\text{COOH}$ ,  $-\text{SO}_3\text{H}$ ,  $-\text{SO}_2\text{HNR}^3$ ,  $-\text{PO}_2(\text{R}^3)_2$ ,  $-\text{CN}$ ,  $-\text{PO}_3(\text{R}^3)_2$ ,  $-\text{OR}^3$ ,  $-\text{SR}^3$ ,  $-\text{NHCOR}^3$ ,  $-\text{N}(\text{R}^3)_2$ ,  $-\text{CON}(\text{R}^3)_2$ ,  $-\text{CONH}(\text{O})\text{R}^3$ ,  $-\text{CONHNHSO}_2\text{R}^3$ ,  $-\text{COHNSO}_2\text{R}^3$ , and  $-\text{CONR}^3\text{CN}$ .

5. The compounds, (2S)-1-(phenylmethyl)sulfonyl-2-hydroxymethyl pyrrolidine; (2S)-1-(phenylmethyl)sulfonyl-2-pyrrolidinetetrazole.

6. A pharmaceutical composition, comprising:

- a) an effective amount of an N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere; and
- b) a pharmaceutically acceptable carrier.

7. The pharmaceutical composition of claim 6, wherein the N-linked sulfonamide of N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



I

where

$n$  is 1-3;

$R_1$  is selected from the group consisting of hydrogen,  $C_1-C_9$  straight or branched chain alkyl,  $C_2-C_9$  straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a  $C_1-C_{10}$  straight or branched chain alkyl,  $C_2-C_{10}$  alkenyl or  $C_2-C_{10}$  alkynyl;

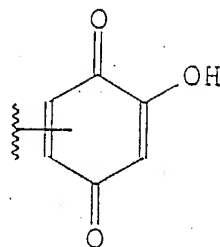
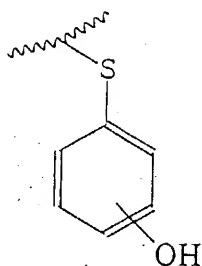
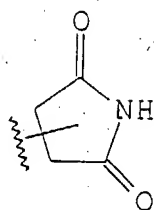
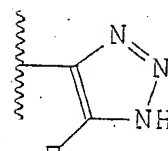
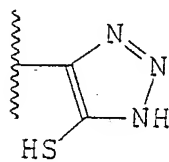
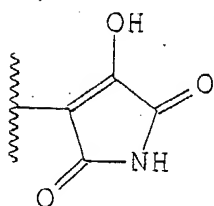
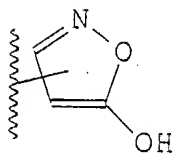
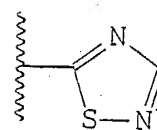
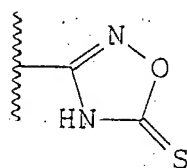
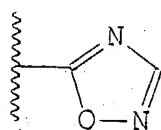
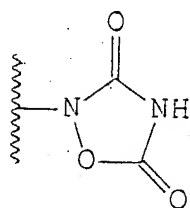
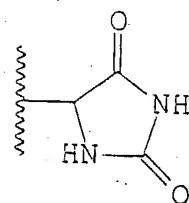
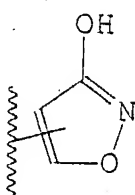
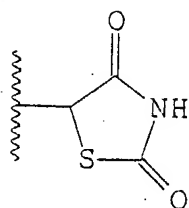
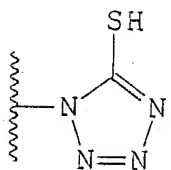
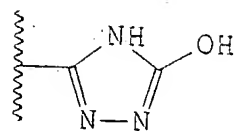
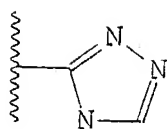
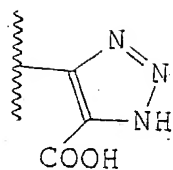
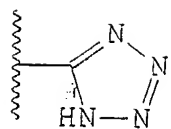
$R_2$  is a carboxylic acid or a carboxylic acid isostere; wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from  $R^3$ , where

$R^3$  is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl,  $C_1-C_6$  straight or branched chain alkyl,  $C_2-C_6$  straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or  $CO_2R^4$  where  $R^4$  is hydrogen or  $C_1-C_9$  straight or branched chain alkyl or alkenyl;

or a pharmaceutically acceptable salt, ester or solvate thereof.

8. The pharmaceutical composition of claim 7, wherein  $R_2$  is a carbocycle or heterocycle containing any combination of  $CH_2$ , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with  $R^3$ .

9. The pharmaceutical composition of claim 7, wherein  $R_2$  is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with R<sup>3</sup>.

10. The pharmaceutical composition of claim 7, wherein  
5 R<sub>2</sub> is selected from the group consisting of:

-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sup>3</sup>, -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>, -OR<sup>3</sup>, -SR<sup>3</sup>, -NHCOR<sup>3</sup>, -N(R<sup>3</sup>)<sub>2</sub>, -CON(R<sup>3</sup>)<sub>2</sub>, -CONH(O)R<sup>3</sup>, -CONHNHSO<sub>2</sub>R<sup>3</sup>, -COHNSO<sub>2</sub>R<sup>3</sup>, and -CONR<sup>3</sup>CN.

10 11. The pharmaceutical composition of claim 7, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid compound is selected from the group consisting of compounds 1-97.

15 12. The pharmaceutical composition of claim 6, further comprising a neurotrophic factor different from formula (I).

20 13. The pharmaceutical composition of claim 12, wherein said neurotrophic factor different from formula (I) is selected from neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3 and neurotrophin 4/5.

14. A method of treating a neurological disorder in an animal, comprising:

30 administering to the animal an effective amount of an N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere to stimulate growth of damaged peripheral nerves or to promote neuronal regeneration.



15. The method of claim 14, wherein the neurological disorder is selected from the group consisting of peripheral neuropathies cause by physical injury or disease state, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, and neurological disorders relating to neurodegeneration.

16. The method of claim 14, wherein the neurological disorder is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, and amyotrophic lateral sclerosis.

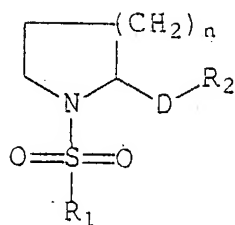
17. The method of claim 14, wherein the neurological disorder is Alzheimer's disease.

18. The method of claim 14, wherein the neurological disorder is Parkinson's disease.

19. The method of claim 14, wherein the neurological disorder is amyotrophic lateral sclerosis.

20. The method of claim 14, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

21. The method of claim 14, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



where

n is 1-3;

R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere;

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or CO<sub>2</sub>R<sup>4</sup> where R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl;

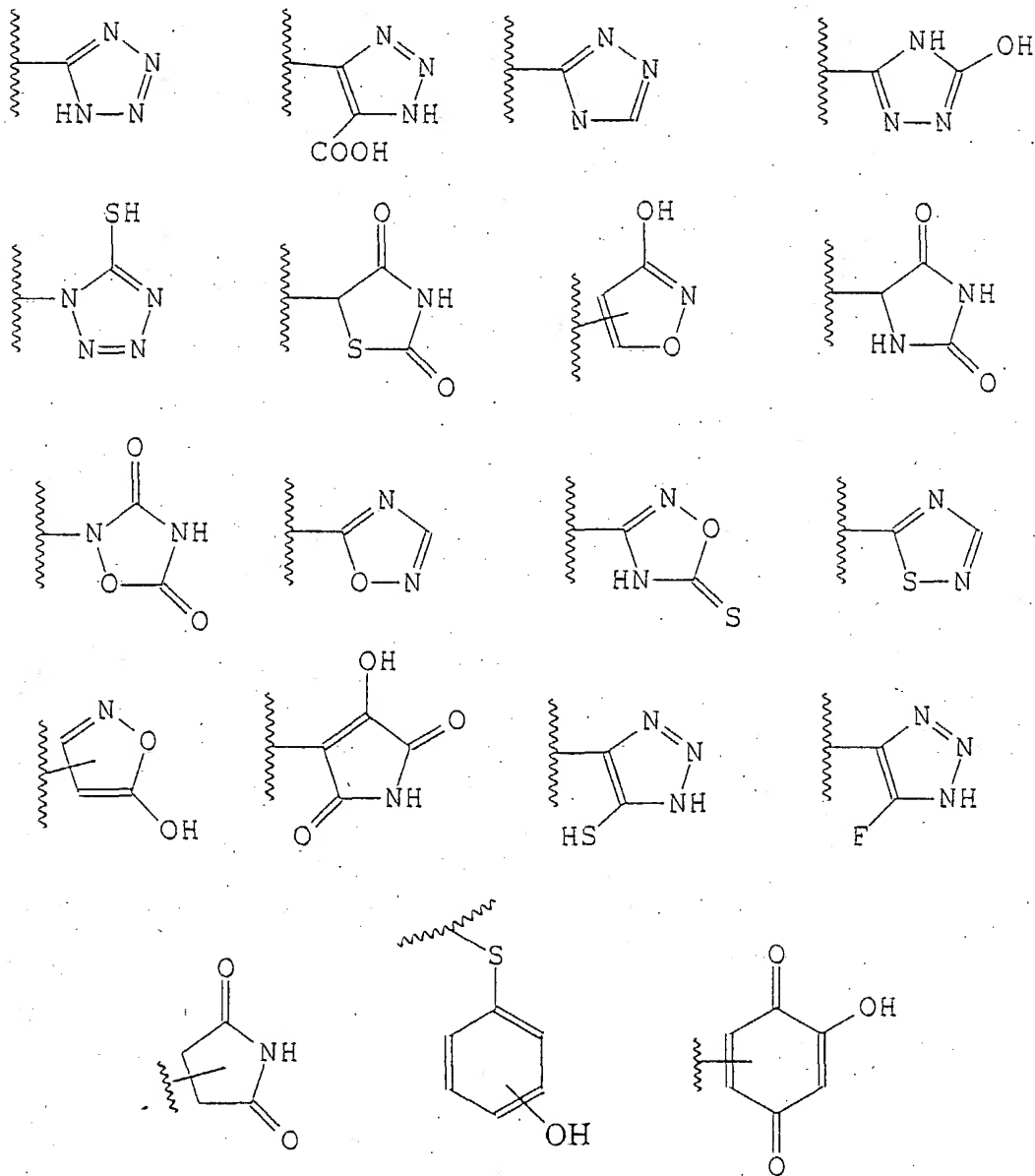
or a pharmaceutically acceptable salt, ester or solvate thereof.

22. The method of claim 21, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein

any of the atoms of said ring structure are optionally substituted in one or more positions with  $R^3$ .

23. The method of claim 21, wherein  $R_2$  is selected from the following group:

5



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

24. The method of claim 21, wherein  $R_2$  is selected from the group consisting of:

-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sup>3</sup>, -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>, -OR<sup>3</sup>, -SR<sup>3</sup>, -NHCOR<sup>3</sup>, -N(R<sup>3</sup>)<sub>2</sub>, -CON(R<sup>3</sup>)<sub>2</sub>, -CONH(O)R<sup>3</sup>, -CONHNHSO<sub>2</sub>R<sup>3</sup>, -COHNSO<sub>2</sub>R<sup>3</sup>, and -CONR<sup>3</sup>CN.

25. The method of claim 14, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid compound is selected from the group consisting of compounds 1-97.

26. The method of claim 14, further comprising administering a neurotrophic factor different from formula (I).

27. The method of claim 26, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

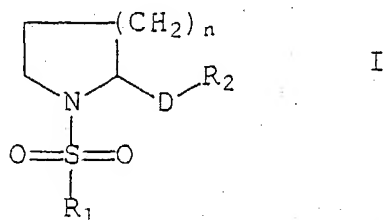
28. A method of stimulating growth of damaged peripheral nerves, comprising:

administering to damaged peripheral nerves a therapeutically effective amount of an N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere to stimulate or promote growth

of the damaged peripheral nerves.

29. The method of claim 28, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

30. The method of claim 28, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



where

n is 1-3;

R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere; wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

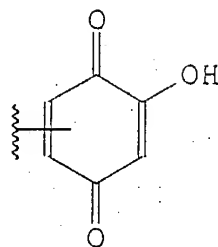
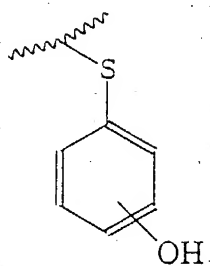
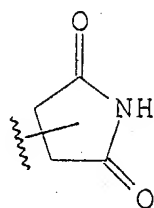
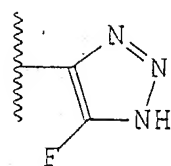
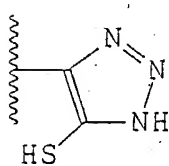
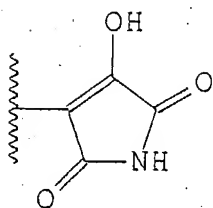
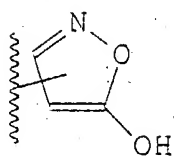
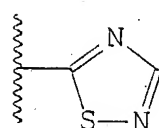
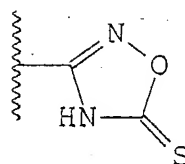
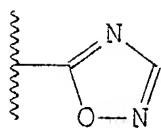
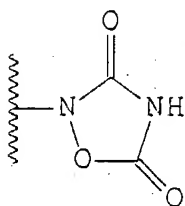
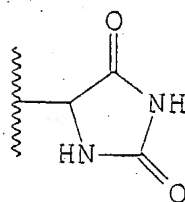
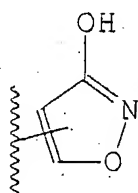
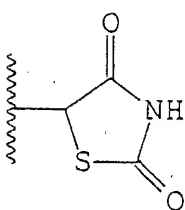
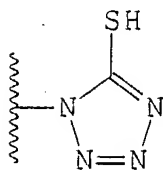
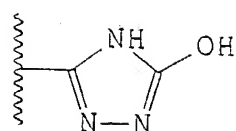
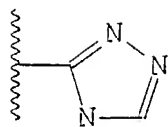
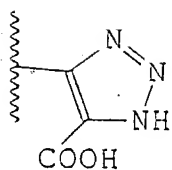
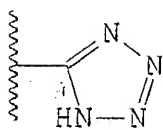
R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or

branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or CO<sub>2</sub>R<sup>4</sup> where R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl or alkenyl;

5 or a pharmaceutically acceptable salt, ester or solvate thereof.

31. The method of claim 30, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein  
10 any of the atoms of said ring structure are optionally substituted in one or more positions with R<sup>3</sup>.

32. The method of claim 30, wherein R<sub>2</sub> is selected from  
15 the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

33. The method of claim 30, wherein  $R_2$  is selected from the group consisting of:

-COOH,  $-SO_3H$ ,  $-SO_2HNR^3$ ,  $-PO_2(R^3)_2$ ,  $-CN$ ,  $-PO_3(R^3)_2$ ,  $-OR^3$ ,  $-SR^3$ ,  $-NHCOR^3$ ,  $-N(R^3)_2$ ,  $-CON(R^3)_2$ ,  $-CONH(O)R^3$ ,  $-CONHNHSO_2R^3$ ,  $-COHNSO_2R^3$ , and  $-CONR^3CN$ .

34. The method of claim 28, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid compound is selected from the group consisting of compounds 1-97.

35. The method of claim 28, further comprising administering a neurotrophic factor different from formula (I).

36. The method of claim 35, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain-derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

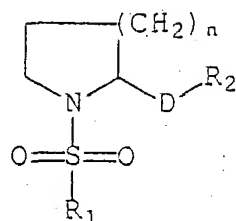
37. A method for promoting neuronal regeneration and growth in animals, comprising:

administering to an animal a therapeutically effective amount of a neurotrophic N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere to promote neuronal regeneration.



38. The method of claim 37, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

39. The method of claim 37, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



where

n is 1-3;

R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere;

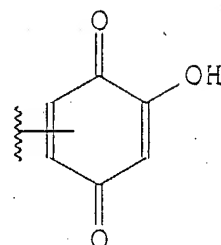
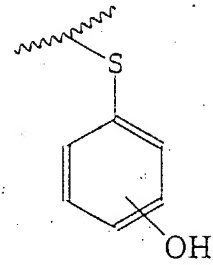
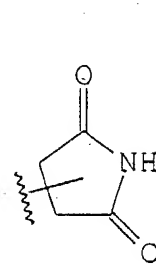
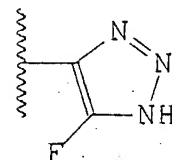
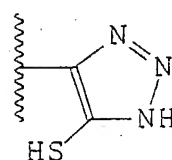
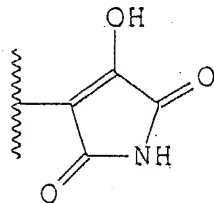
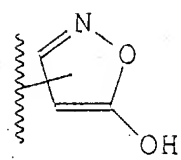
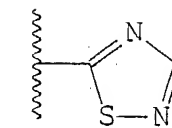
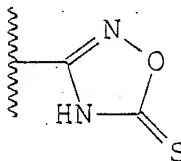
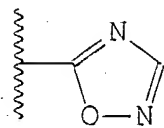
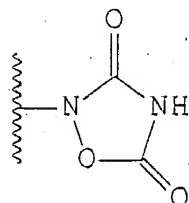
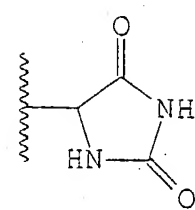
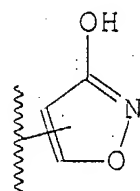
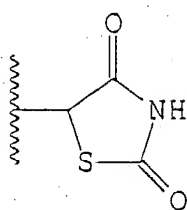
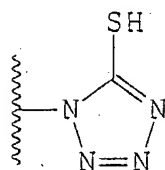
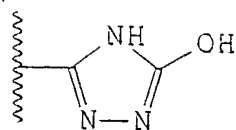
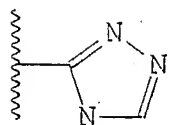
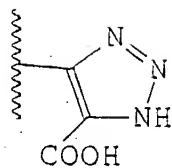
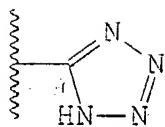
wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle,

heterocycle, or  $\text{CO}_2\text{R}^4$  where  $\text{R}^4$  is hydrogen or  $\text{C}_1\text{-C}_9$  straight or branched chain alkyl or alkenyl; or a pharmaceutically acceptable salt, ester or solvate thereof.

5  
40. The method of claim 39, wherein  $\text{R}_2$  is a carbocycle or heterocycle containing any combination of  $\text{CH}_2$ , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with  $\text{R}^3$ .  
10

41. The method of claim 39, wherein  $\text{R}_2$  is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^1$ .

42. The method of claim 39, wherein  $R_2$  is selected from the group consisting of:

-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sup>3</sup>, -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>, -OR<sup>3</sup>, -SR<sup>3</sup>, -NHCOR<sup>3</sup>, -N(R<sup>3</sup>)<sub>2</sub>, -CON(R<sup>3</sup>)<sub>2</sub>, -CONH(O)R<sup>3</sup>, -CONHNHSO<sub>2</sub>R<sup>3</sup>, -COHNSO<sub>2</sub>R<sup>3</sup>, and -CONR<sup>3</sup>CN.

43. The method of claim 37, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid compound is selected from the group consisting of compounds 1-97.

44. The method of claim 37, further comprising administering a neurotrophic factor different from formula (I).

45. The method of claim 44, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof; acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

46. A method for preventing neurodegeneration in an animal, comprising:

administering to an animal a therapeutically effective amount of a neurotrophic N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere to prevent neurodegeneration.

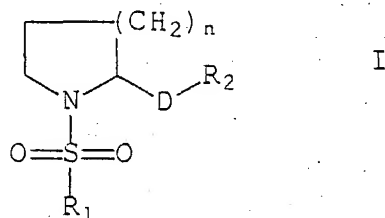
47. The method of claim 46, wherein the neurodegeneration is Alzheimer's disease.

48. The method of claim 46, wherein the neurodegeneration is Parkinson's disease.

49. The method of claim 46, wherein the neurodegeneration is amyotrophic lateral sclerosis.

50. The method of claim 46, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

51. The method of claim 46, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



where

n is 1-3;

R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere;

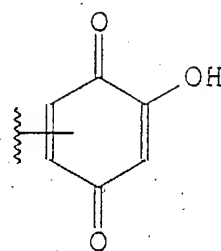
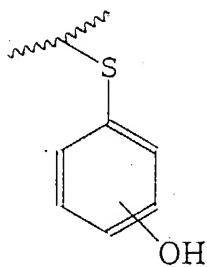
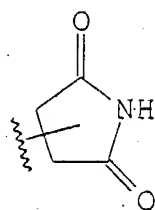
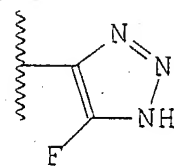
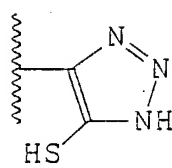
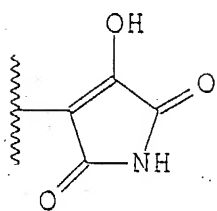
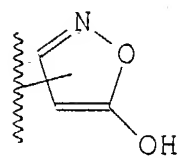
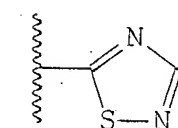
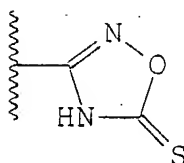
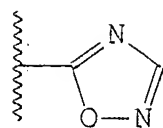
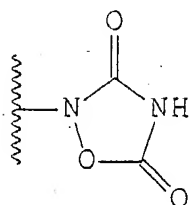
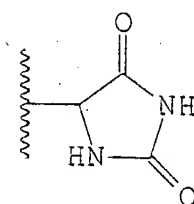
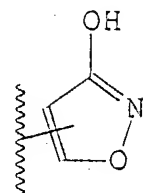
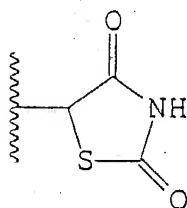
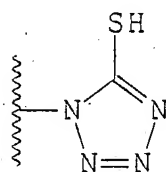
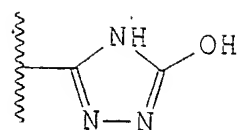
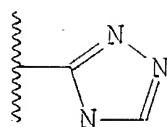
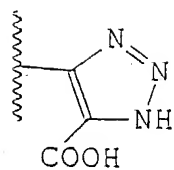
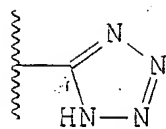
wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl,

carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from  $R^3$ , where

$R^3$  is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl,  $C_1-C_6$  straight or branched chain alkyl,  $C_2-C_6$  straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or  $CO_2R^4$  where  $R^4$  is hydrogen or  $C_1-C_9$  straight or branched chain alkyl or alkenyl; or a pharmaceutically acceptable salt, ester or solvate thereof.

52. The method of claim 51, wherein  $R_2$  is a carbocycle or heterocycle containing any combination of  $CH_2$ , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with  $R^3$ .

53. The method of claim 51, wherein  $R_2$  is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with R<sup>3</sup>.

5 54. The method of claim 51, wherein R<sub>2</sub> is selected from the group consisting of:

-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sup>3</sup>, -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>, -OR<sup>3</sup>, -SR<sup>3</sup>, -NHCOR<sup>3</sup>, -N(R<sup>3</sup>)<sub>2</sub>, -CON(R<sup>3</sup>)<sub>2</sub>, -CONH(O)R<sup>3</sup>, -CONHNHSO<sub>2</sub>R<sup>3</sup>, -COHNSO<sub>2</sub>R<sup>3</sup>, and -CONR<sup>3</sup>CN.

10 55. The method of claim 46, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid compound is selected from the group consisting of compounds 1-97.

15 56. The method of claim 46, further comprising administering a neurotrophic factor different from formula (I).

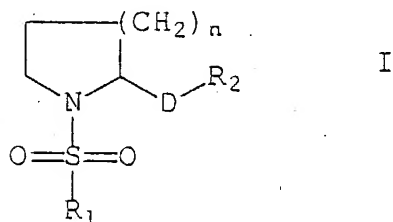
20 57. The method of claim 56, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

30 58. A method for treating alopecia or promoting hair growth in an animal, which comprises administering to said animal an effective amount of an N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere.



59. The method of claim 58, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

60. The method of claim 58, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere is a compound of formula (I):



where

n is 1-3;

R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

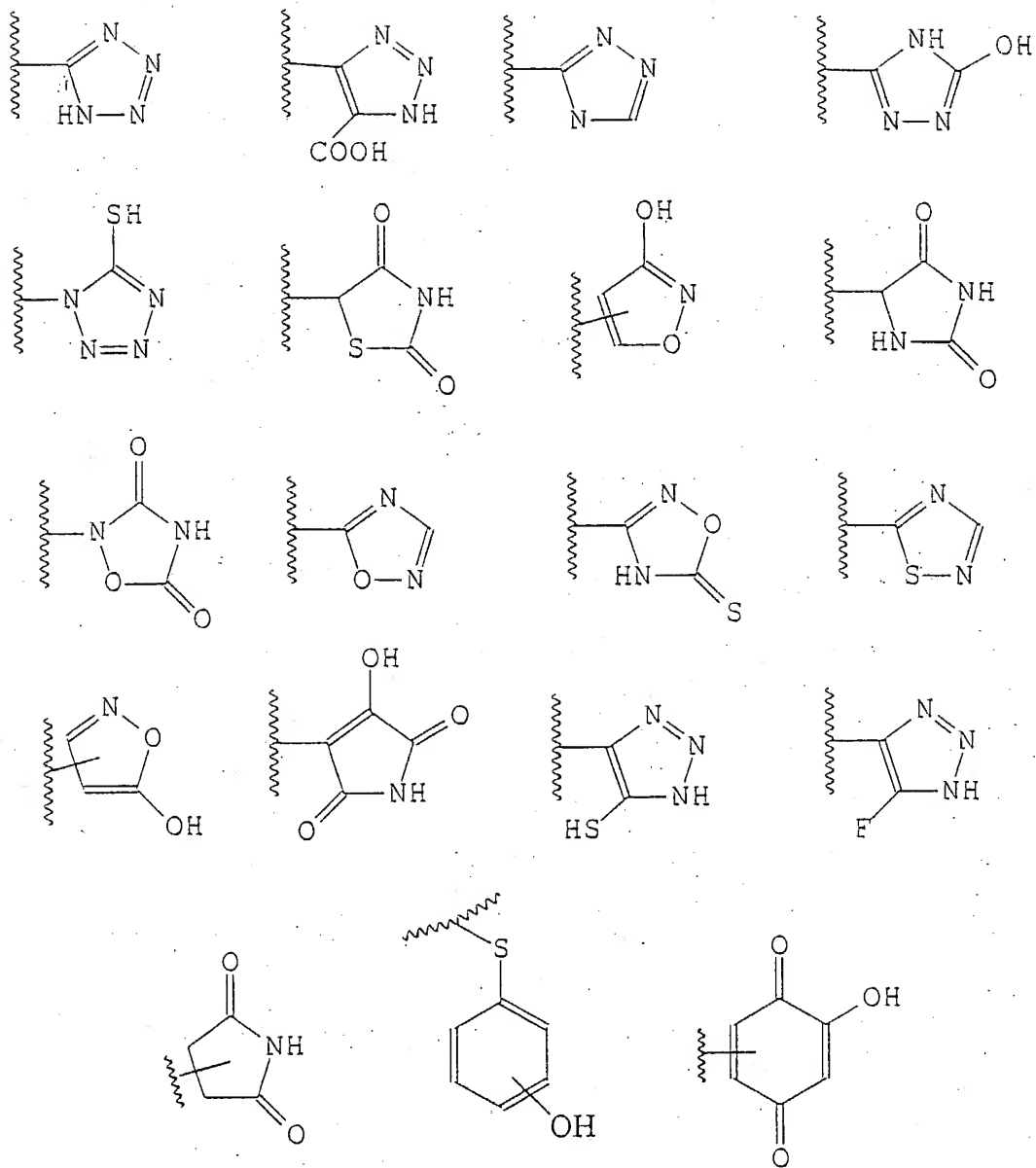
R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere; wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or CO<sub>2</sub>R<sup>4</sup> where R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub>,

straight or branched chain alkyl or alkenyl;  
or a pharmaceutically acceptable salt, ester or solvate  
thereof.

5 61. The method of claim 60, wherein  $R_2$  is a carbocycle  
or heterocycle containing any combination of  $CH_2$ , O, S,  
or N in any chemically stable oxidation state, wherein  
any of the atoms of said ring structure are optionally  
substituted in one or more positions with  $R^3$ .

10 62. The method of claim 60, wherein  $R_2$  is selected from  
the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

63. The method of claim 60, wherein  $R_2$  is selected from the group consisting of

-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sup>3</sup>, -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>, -OR<sup>3</sup>, -SR<sup>3</sup>, -NHCOR<sup>3</sup>, -N(R<sup>3</sup>)<sub>2</sub>, -CON(R<sup>3</sup>)<sub>2</sub>, -CONH(O)R<sup>3</sup>, -CONHNHSO<sub>2</sub>R<sup>3</sup>, -COHNSO<sub>2</sub>R<sup>3</sup>, and -CONR<sup>3</sup>CN.

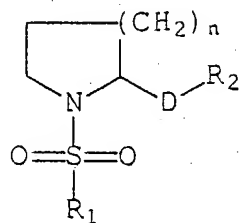
64. The method of claim 58, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-97.

65. A pharmaceutical composition comprising:

- (i) an effective amount of a N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere for treating alopecia or promoting hair growth in an animal; and
- (ii) a pharmaceutically acceptable carrier.

66. The pharmaceutical composition of claim 65, wherein the N-linked sulfonamide of an N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

67. The composition of claim 65, wherein the carboxylic acid or carboxylic acid isostere is a compound of formula (I):



I

where

n is 1-3;

R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere;

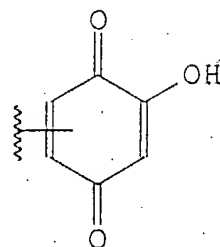
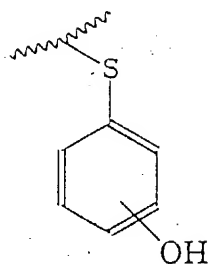
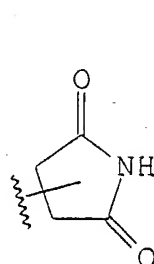
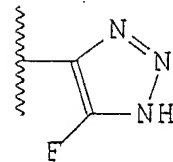
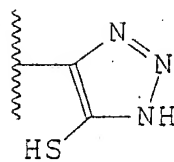
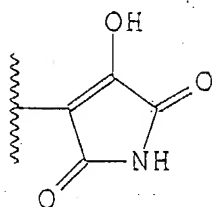
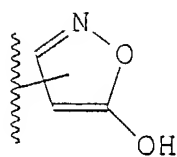
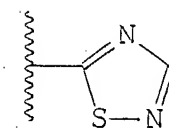
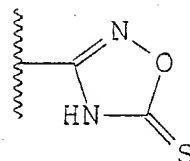
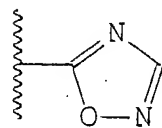
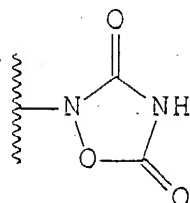
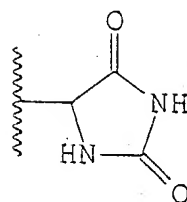
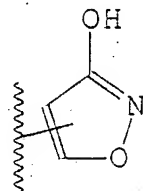
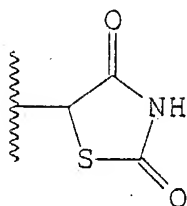
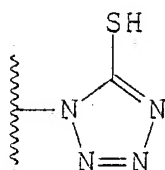
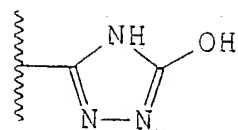
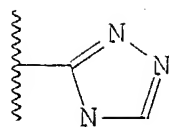
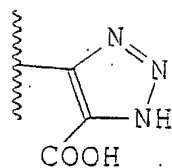
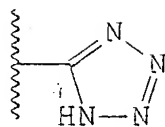
wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or CO<sub>2</sub>R<sup>4</sup> where R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl;

or a pharmaceutically acceptable salt, ester or solvate thereof.

68. The composition of claim 67, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R<sup>3</sup>.

69. The composition of claim 67, wherein R<sub>2</sub> is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

5 70. The composition of claim 67, wherein  $R_2$  is selected from the group consisting of:

-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sup>3</sup>, -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>, -OR<sup>3</sup>, -SR<sup>3</sup>, -NHCOR<sup>3</sup>, -N(R<sup>3</sup>)<sub>2</sub>, -CON(R<sup>3</sup>)<sub>2</sub>, -CONH(O)R<sup>3</sup>, -CONHNHSO<sub>2</sub>R<sup>3</sup>, -COHNSO<sub>2</sub>R<sup>3</sup>, and -CONR<sup>3</sup>CN.

10 71. The composition of claim 65, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-97.